Intravenous Ether Anesthesia

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• **From a study of intravenous ether anesthesia, it was concluded that ether diluted to a 5 per cent solution in 5 per cent dextrose and water may be used to induce and maintain a smooth and easily controlled anesthetic state similar to that obtained with inhalation ether but without the dependence of the latter technique on ventilation. Cough and laryngospasm were absent. Adequate spontaneous respiration can be maintained with this technique. The technique is particularly useful in endoscopy during which the airway is often not available for anesthetic administration.**

THE INDUCTION and maintenance of anesthesia by injection of drugs intravenously has several advantages over that produced by inhalation of gases or vapors. The distress and fear associated with a face mask is eliminated, and the impact of irritating vapors on protective reflexes is avoided. Ventilation does not limit the rate at which induction is achieved nor the rate at which anesthetic depth is increased. The depth of anesthesia may be maintained or altered even in apneic patients.

These advantages are of particular value in laryngoscopy and bronchoscopy, for in those procedures the respiratory tract of the patient must be shared by surgeon and anesthetist, with the anesthetist sometimes excluded. Hence ventilation during endoscopy is often interrupted or compromised and inhalation anesthetic agents introduced into the respiratory tract may be removed by suction or diluted by room air. Anesthetic vapor is often irritating to the endoscopist, and the combination of vapor and room air sometimes produces refractions which obscure his view.

Two classes of anesthetic drugs are often given intravenously: the barbiturates and the narcotics. These drugs have several serious drawbacks. Barbiturates produce hypnosis but not analgesia except with doses that produce profound respiratory and circulatory depression. Narcotics, as commonly used, produce analgesia but inadequate hypnosis. If enough is given to bring about hypnosis, profound respiratory and circulatory depression may result. The combining of barbiturate and narcotic does not eliminate the hazards associated with their individual use. In addition, an overdose of these agents cannot be readily eliminated as can agents that are eliminated through the lungs. An inhalation agent given intravenously might possess the advantages of both techniques. Several inhalation agents may be given by vein but usually require fat emulsions as a solvent.[16] However, diethyl ether can be dissolved in adequate concentrations in any of the solutions commonly given intravenously.

The use of ether intravenously was extensively investigated by Burkhardt in 1909 and 1911.[3,4,5] He found that anesthesia could be induced in 8 to 10 minutes with 300 to 600 ml of a 5 per cent (volume in volume) solution of ether in saline solution. Concentrations greater than 5 per cent produced hemolysis and thrombophlebitis and lesser concentrations necessitated introducing undesirably large total volumes. The anesthetic course was uneventful and no adverse circulatory or respiratory effects were noted. Postoperative vomiting was rare. Thrombophlebitis occurred infrequently despite the use of a cut-down and cannula. No untoward effects were found even in seriously ill patients. No cases of pulmonary edema were noted in these or other reports despite the volumes injected. Burkhardt suggested, however, that ether should not be given intravenously to plethoric, anemic, nephritic or arteriosclerotic patients. Following his reports, several similar studies were published confirming most of his observations.* However, Dieterich[7] found excitement on induction and other investigators noted postoperative thrombosis to be frequent.[14,21] After 1914 interest in this technique waned and few subsequent publications on its use can be found.[7,9,22]

Recently we reinvestigated intravenous ether anesthesia. Our work was divided into two parts: (1) reconfirmation of the results initially obtained by Burkhardt and (2) application of the technique to bronchoscopy and laryngoscopy, where we felt it might be of particular value.

To determine the concentration of ether which caused hemolysis, blood was mixed with an equal

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*References 1, 2, 7, 8, 11, 13-15, 17-19, 21, 22.

volume of ether solutions of various concentrations and allowed to stand for 10 minutes. Plasma was then separated by centrifugation and observed for gross hemolysis. No hemolysis was apparent with 5 per cent ether but a slight amount was detected at 6 per cent and an increasing amount as concentration increased beyond this point.

Fifty patients were selected for study. The technique was not used if (1) a flammable anesthetic was contraindicated or (2) the patient was in congestive or renal failure. Patients' ages ranged from 4 to 68 years, and there were 31 females and 19 males. Preanesthetic medication consisted of pentobarbital and/or a narcotic (usually morphine) and/or a vagolytic (atropine or scopolamine). Dosage was varied to suit patient age and physical status.

Ether was dissolved in 0.9 per cent saline solution or in 5 per cent dextrose in water. When we gave large volumes (1,500-2,000 ml) of saline in one to two hours, the mucous membranes of the eyes and mouth often appeared edematous. No other untoward effect was noted. With dextrose solution, edema was not seen. The solutions were refrigerated before mixing and were often still cold when injected. The volume of ether (Squibb) to be added to the solution to make a 5 per cent (volume in volume) solution was determined by multiplying the volume of solution by 0.0526. For example, 52.6 ml of ether was added to exactly one liter of dextrose solution. After the ether was added, the flask was vigorously shaken until the ether could no longer be seen as a layer at the top. An intravenous infusion was started with a needle sufficiently large (15 to 18 gauge) so that the solution could flow as a stream rather than as individual drops. Before injection, a heparinized blood specimen was drawn for a control. In several cases electroencephalographic (EEG) tracings were taken as the ether solution was started and were continued throughout the procedure. Thiobarbiturate (200 to 400 mg) was usually given before starting ether. When ether solution was used for induction without previous administration of a barbiturate, patients complained of pain in the vein used. Most of the pain could be eliminated by warming the solution or by injecting 100 mg of lidocaine through the needle and holding it at the site of injection for 2 to 3 minutes by use of a tourniquet. Even with pain eliminated, induction with ether alone was often marred by excitement. With the infusion running freely plane 2, stage 3 or EEG level IV was reached in 5 to 15 minutes after injection of 250 to 600 ml of solution (Figure 1). Much more rapid onset of anesthesia could be obtained if the ether solution was infused under pressure (Figure 2). Stage IV could be

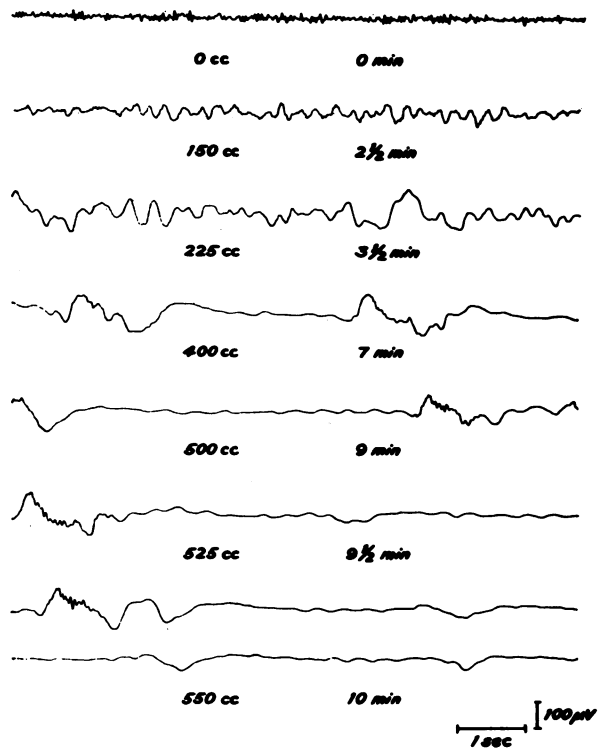

Figure 1.—A typical electroencephalogram recording with 5 per cent ether administered as rapidly as it would flow through a 16 gauge needle. At 0 minutes a level I recording of low voltage-high frequency was seen. After 2½ minutes infusion of 150 cc produced a change to level II or III. After 3½ minutes and 225 cc a level III pattern (a chaotic pattern of high voltage-low frequency) was noted. By 7 minutes 400 cc had been administered and an electroencephalogram level IV (a chaotic pattern of high voltage-low frequency with 1 to 3 seconds of burst suppression) was reached. Level V (same as level IV but with 3 to 10 seconds of burst suppression) was attained at 9 minutes after infusion of 500 cc. Level VI (same as level IV but with burst suppression longer than 10 seconds) and level VII (isoelectric electroencephalogram) was reached at 10 minutes after administration of 550 cc of ether solution.

reached in 2 to 4 minutes under these conditions. However, this accelerated induction was often accompanied by hypotension. EEG changes paralleled clinical signs of anesthesia and were similar to the patterns described by Courtin and coworkers[6] for inhalation ether. If the infusion was stopped after EEG level IV was attained, the EEG trace rapidly returned to level I (Figure 2 and 3). Although excitement occurred with ether induction, coughing and laryngospasm were not problems regardless of the rate of infusion, nor was the odor of ether offensive to the patient.

After induction, the patient was allowed to breathe oxygen or oxygen-nitrous oxide via a face mask from a semi-closed or closed circle system. Ventilation often appeared depressed and was assisted or controlled if necessary. Anesthesia could

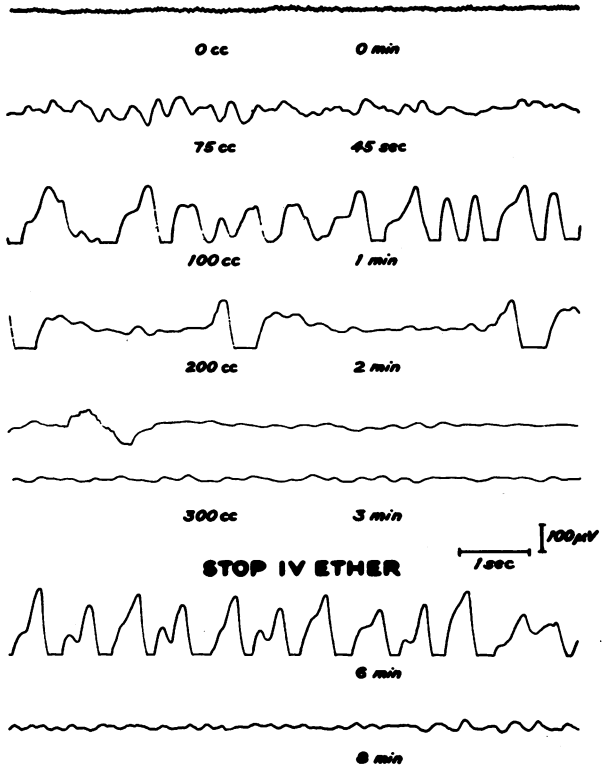

Figure 2.—In this experiment the ether solution was injected as rapidly as possible with a syringe through an 18 gauge needle. Initially a level I electroencephalogram tracing was seen. By 45 seconds this had changed to level II or III and by 1 minute to a definite level III. Level IV was reached in 2 minutes, and by 3 minutes level VI or VII was attained. The patient was apneic and hypotensive at this time and the infusion was halted. Three minutes later a level III record was attained and 2 minutes after this (8 minutes after the start of the ether infusion) a level II or I pattern reappeared. By this time the patient's vital signs had returned to normal.

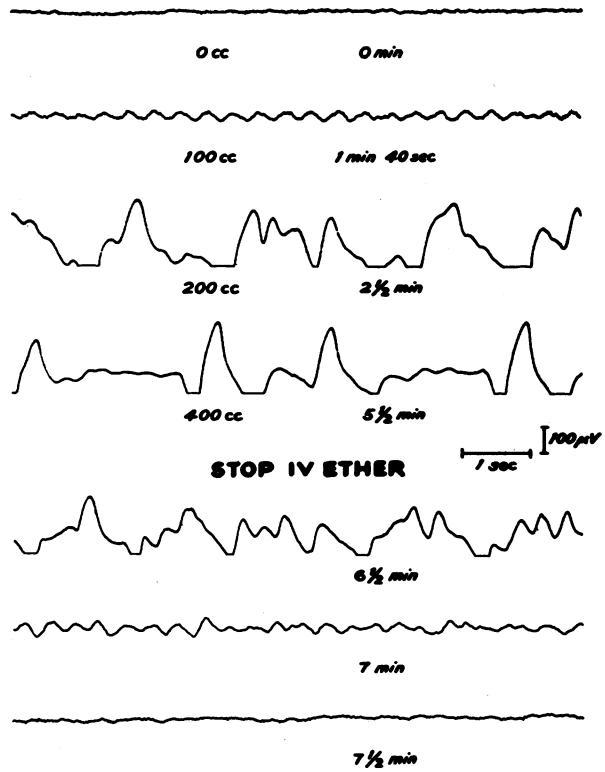

Figure 3.—Ether solution was allowed to flow (16 gauge needle) in this case until level IV was reached. Infusion was halted at this time to show the rapid recovery that occurs before saturation of the body with ether. At 0 time a level I pattern was seen. By 1 minute 40 seconds, level II (rhythmical low frequency waves of 100-200 microvolts amplitude) was obtained. Level III was reached in 2½ minutes and level IV at 5½ minutes after administration of 400 cc of solution. The ether infusion was stopped at 5½ minutes and by 6½ minutes had returned to level III; by 7 minutes to level II; and by 7½ minutes to level I.

be maintained at any desired level[9] and could be made sufficient for all surgical procedures. Although respiration appeared somewhat depressed, circulation as measured by blood pressure remained adequate unless infusion was very rapid. The rate of infusion required for maintenance of anesthesia (500 to 1,000 ml in the first hour) was considerably less per unit time than that required for induction.[9] In addition, the maintenance requirements themselves fell as time passed (300 to 500 ml was required during the second hour).

At the end of the procedure a heparinized blood specimen was drawn. The plasma from this sample was compared for gross hemolysis with that taken before induction. In one case slight hemolysis was noted. In this case, 6 per cent ether had been used due to an error in calculation. The urine was examined after anesthesia in all cases. In no case was gross hemoglobinuria found. Twenty of the 50 patients (40 per cent) were nauseated post anesthetically and 18 vomited (36 per cent). If the patients are divided into those who received less than 1,000 ml of solution (26 patients or 52 per cent) and those who received more than 1,000 ml (24 or 48 per cent) a striking difference was found in incidence of nausea and vomiting. Of those who received less than 1,000 ml, three (12 per cent) were nauseated and one (4 per cent) vomited. Of those who received more than 1,000 ml, 16 (66 per cent) were nauseated and vomited. Three patients (6 per cent) had post operative phlebitis at the infusion site and three others had thrombophlebitis. Hot packs were applied to the affected area and all recovered without incident.

It was noted that pure ether dissolved the plastic material used in disposable infusion sets and syringes. It was not known whether the ether solutions would act similarly. To test this, the infusion tubing used in nine cases was rinsed with water and dried with suction. The average weight of these tubes

was compared with the average of four unused sets. No difference was found between the two groups.

Bronchoscopy or laryngoscopy was the operative procedure for 20 of the 50 patients. The anesthetic management was slightly altered in these patients. Pre-anesthetic preparation and induction were similar, but after induction the larynx and trachea were topically anesthetized either by translaryngeal injection or by spray during direct laryngoscopy (under the intravenous ether anesthesia). The latter approach to topical anesthesia had the advantage of aiding in the evaluation of the adequacy of anesthesia for endoscopy. Following the topical application, anesthesia was deepened if necessary. Endoscopy was accomplished without difficulty in 17 of the cases. In three cases the masseter muscles remained tense despite anesthesia almost to the point of apnea. In these cases, a very small dose of curare (1-3 mg) produced adequate relaxation. Occasionally, despite the topical anesthesia, the patient would react to instrumentation by coughing. Giving additional ether overcame this difficulty, but 25 to 50 mg of thiopental usually produced the desired result more rapidly. Larger doses of barbiturate (50 to 100 mg) often produced apnea. Although ventilation appeared adequate in most cases, oxygen was insufflated to diminish any possibility of hypoxia. The range between the amount of anesthetic that produced adequate conditions for endoscopy and that which produced significant respiratory depression appeared to be narrower than with inhalation ether. This may be because an anesthetic given intravenously is not subject to the limitation that decreased ventilation imposes on further deepening with an inhalation anesthetic.

The use of intravenous ether anesthesia for endoscopy has been well received both by surgeons and anesthetists. Although it is not a perfect anesthetic it does not have many of the hazards of other techniques. For example, when intravenous barbiturates and muscle relaxants are used, the time for endoscopy must be limited lest hypoxia and hypercarbia occur.[10] If cuirass or chest respirator[12] is used in addition, then ventilation may be adequate but is difficult to monitor visually or by auscultation. Either case involves the use of fixed agents which cannot be eliminated via the respiratory tract. Insufflation of general anesthetic agents entails difficulties already mentioned. The administration of inhalation anesthetics through a small endotracheal tube rather than by insufflation results in a great reduction in airway diameter and hence an increase in resistance to breathing.[26] In addition the tube may obstruct the view of the endoscopist.

In comparison with the drawbacks associated with these techniques, ether anesthesia given by vein produces a stable level of anesthesia which is adequate for prolonged endoscopy (15 to 30 minutes). Ventilation during this period remains adequate. Equally important is that ventilation can be monitored visually or by auscultation. Although there is ether in the exhaled air, it is not of great enough concentration to be irritating or cause refractive problems. Elimination of the agent may be accelerated by hyperventilation. Nausea and vomiting are infrequent if less than 1,000 ml of solution is used.

The technique has some obvious drawbacks. Some of these are inherent in the agent, ether: (1) fairly long recovery if saturation has occurred, (2) post operative nausea and vomiting and (3) flammability. Flammability is a lesser problem with this technique than with ether insufflation, in which concentrations of 10 to 30 per cent may be required. With the intravenous route, the highest exhaled concentrations are between 3 and 6 per cent and approach the lower limit of flammability. Other drawbacks include: (1) a narrow range between adequate anesthesia and depressed respiration; (2) a moderately long period of induction: Ten minutes is about average and 15 to 20 minutes may be required if the intravenous flow is not rapid enough; and (3) administration of a fairly large volume of solution (1 to 1.5 liters) intravenously in a short time (one hour).

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CORRECTION

A MISSTATEMENT of the strength of a drug solution appeared in the article *Insect Sting Anaphylaxis* which was published in the September issue of CALIFORNIA MEDICINE.

The error is on page 170, in item (d) under the subhead *Second Stage Treatment.* The second sentence of item (d) should read: Chlorpheniramine maleate (Chlor-Trimeton®, 10 mg per cc) . . .

As it appeared, the amount was given erroneously as 100 mg per cc.